

Occupational Cancer in Spain

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The knowledge of specific problems of occupational cancer in Spain is scarce. The environment of the workplace has improved over the last few years after a long period distinguished by bad working conditions, incomplete legislation, and insufficient safety measures and control. It has been estimated that 3,083,479 workers (25.4% of employees) were exposed to carcinogens. The most common occupational exposures to carcinogenic agents were solar radiation, environmental tobacco smoke, silica, and wood dust. The highest number of employees were exposed to silica crystalline (404,729), diesel engine exhaust (274,321), rubber products (99,804), benzene (89,932), ethylene dibromide (81,336), agents used in furniture and cabinet making (72,068), and formaldehyde (71,189). The percentage of total cancer deaths attributed to occupational exposure was 4% (6% in men, 0.9% in women). Compared with other European countries, the incidence of lung cancer and leukemia in Spain are one of the lowest, but it is rapidly increasing. The incidence of urinary bladder and larynx cancer, on the contrary, are one of the highest. Few studies on occupational cancer have been conducted in Spain. The main problems are the availability of death certificates and the quality of the information on occupation in mortality of statistics. It is necessary to improve methods of assessment of exposures using expert hygienists and biologic markers of exposure and diseases. Reduction of cancer by limiting or avoiding exposure to known occupational carcinogens is still necessary. — *Environ Health Perspect* 107(Suppl 2):273–277 (1999). <http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/273-277gonzalez/abstract.html>

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Occupational cancer research in Spain is a developing field, which still in its initial phase. The knowledge of specific problems of occupational cancer in our country is scarce. Modern epidemiology has been established very recently in Spain and the contribution of Spanish epidemiology to the identification of occupational risk factors and the evaluation of the impact of occupational cancer risk is very limited.

These limitations in research have been accompanied by many problems in working conditions, incomplete legislation, and insufficient control and safety measures in the working environment, although the situation has improved in the last few years after a very long transition period. The European Directive (89/391/CEE) on Prevention of Occupational Risks was included in Spanish legislation in 1995

(1); the European Directive (90/394/CEE) concerning protection of workers from risks related to exposure to carcinogens at work, promulgated in 1990, was adopted in Spanish legislation in 1997 (2).

This article briefly describes the number of subjects exposed to carcinogenic substances in the workplace and presents an estimation of the proportion of cancer attributable to occupational exposure. Also included are the occurrence and trends of cancer types most often associated with occupational exposures, the epidemiologic studies on occupational cancer conducted in Spain, and finally, some reflections on the main problems and challenges for the future.

Number of Subjects Exposed to Carcinogenic Substances at Work

Registration of recognized carcinogens in the workplace is not being carried out in Spain. Accurate information on the number of exposed subjects is not available, but recently (3), using the International Information System on Occupational Exposure to Carcinogens (CAREX), an estimation was made. According to this estimation, there were 12,162,830 employees between 1991 and 1993 in Spain; 3,083,479 (25.4%) of those employees

were exposed to agents that are or could be carcinogenic in humans. The most important industries were construction (677,449 exposed workers) and agriculture (357,740), and the most common occupational exposures to carcinogenic agents were solar radiation, environmental tobacco smoke, silica, and wood dust.

The number of employees exposed to agents present in industrial processes and occupations, which have been classified by the International Agency for Research on Cancer (IARC) (4) into Group 1 (human carcinogens) and Group 2A (probable human carcinogens) according to estimations given by Garcia and Kogevinas (5) and by the CAREX system (3), is shown in Table 1.

The highest number of employees were exposed to silica crystalline (404,729), diesel engine exhaust (274,321), rubber products (99,804), benzene (89,932), ethylene dibromide (81,336), agents used in furniture and cabinet making (72,068), and formaldehyde (71,189).

Asbestos is considered to be the most important occupational carcinogen in Europe, even though its use is decreasing (6). The decrease of domestic consumption of asbestos in Spain is very evident. The importation of asbestos was 112,522 tons in 1973 (7), and decreased to 39,609 tons in 1990 (8). The permitted exposure level to asbestos was fixed at 1 fiber per milliliter air (f/ml) or less in 1984 and the industrial use of blue asbestos was prohibited in 1987 (7,8).

There was also a decrease in the number of enterprises using asbestos and in the number of exposed workers. According to official information (8), in 1984 there were 56 enterprises and 13,645 exposed workers in Spain, whereas in 1991 there were 48 enterprises and 6048 exposed workers. For the same period, the concentration level of asbestos fibers went down from a mean of 2.4 f/ml to 0.22 f/ml (8). According to the estimation using the CAREX system (3) the number of employees exposed to asbestos in 1991 to 1993 in Spain was 56,601.

Despite the fact that agriculture is one of the economic activities with the greatest number of exposed workers, as far as we know there is no estimation of the number

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Abbreviations used: CAREX, International Information System on Occupational Exposure to Carcinogens; CL, confidence limits; IARC, International Agency for Research on Cancer; OR, odds ratio; SMRs, standard mortality ratios.

Table 1. Estimation of exposed employees in Spain by IARC Group 1 and Group 2A carcinogens.^a

Group	Number of exposed, 1991–1993
Group 1 (carcinogenic to humans)	
Aluminium production	3,958
Arsenic and arsenic compounds	11,747
Asbestos	56,601
Auramin, and magenta manufacture	1,671
Benzene	89,932
Benzidine	476
Beryllium and beryllium compounds	3,130
Boot and shoes manufacture and repair	28,985
Cadmium and cadmium compounds	15,988
Chromium VI compounds	56,764
Coal gasification	7,518
Coke production	128
Ethylene oxide	1,093
2-Naphthylamine	163
Furniture and cabinet making	72,068
Hematite mining	1,718
Iron and steel foundry	13,617
Nickel compounds	42,640
Paint	
In activities connected with furniture making	4,211
Construction industry	15,339
In production and repair of vehicles, motorcycles, and cycle repair	14,952
Rubber industry	99,804
Talc containing asbestiform fibers	4,719
Vinyl chloride	1,857
Group 2A (probably carcinogenic to humans)	
Acrylonitrile	1,405
Benzidine-based dyes	427
<i>p</i> -Chloro- <i>o</i> -toluidine and its strong acids salts	32
Diesel engine exhaust	274,321
Dimethyl sulfate	522
Ethylene dibromide	81,336
Formaldehyde	71,189
4,4'-Methylenbis(2-chloroaniline)	245
<i>N</i> -Nitrosodimethylamine	247
Polychlorinated biphenyls	383
Silica, crystalline	404,729
Styrene 7,8-oxide	8,948
Petroleum refining	9,490

^aData modified from Kogevinas (3) and Garcia and Kogevinas (5).

of employees exposed to pesticides in Spain. The consumption of pesticides in Spain has increased from 18,000 million pesetas in 1980 to 64,911 million in 1990 (9). In several areas of Spain—Almeria, Murcia, the Canary Islands, Valencia, Vizcaya, Guipúzcoa, and Catalonia—covered crops are extensive, with considerable exposure to pesticides (organophosphorus, chorophenols, phenoxyacids, arsenic compounds). In Almeria alone, which has 20,000 hectares of greenhouses, there were 60,000 workers exposed to pesticides (10). In the most concentrated covered flower-growing and agricultural production area in Catalonia, in which copious amounts of herbicides and pesticides are used, there were 9551 exposed workers (9); 72.8% of the farmworkers had inadequate protection, and 79.3% said they had suffered symptoms related to pesticide use on some occasion (11).

Estimation of the Proportion of Cancer Related to Occupational Exposures

Following the approach that has been applied by Doll and Peto in the United States (12), it was estimated (5) that in 1991 in Spain a total of 3011 cancer deaths in males and 272 cancer deaths in females were associated with occupational exposures. In men, 65% of total deaths linked to occupational exposures result in lung cancer and 8.7% to bladder cancer. The percentage of total cancer deaths attributed to occupational exposure was 4% (6% in men and 0.9% in women).

Estimation of the proportion of cancers attributable to occupation based on local measures of the level of risk and the proportion of exposed population are not

available in Spain, with two exceptions—a multicenter study on occupation and bladder cancer (13) and a study on bladder cancer in Mataró, an area of Catalonia with a high concentration of textile factories (14).

In the multicenter study, the proportion of bladder cancer cases attributable to occupational exposure was 12%. This estimate is close to the values observed in studies in other countries (15) and indicates that one in eight cases of bladder cancer that occurred in the source population could have been avoided by controlling occupational exposure. The study was conducted in five provinces of Spain—Barcelona, Cadiz, Madrid, Guipúzcoa, and Vizcaya—and the prevalent risk exposures were mainly from the textile, mechanical, and graphics industries. For the Mataró area, it was estimated that exposure in the textile industry may be responsible for 16% of bladder cancer cases (14).

Occurrence and Trends of Some Types of Cancer

When considering the occurrence and trends in males of cancer types most often associated (12) with occupational exposures (lung cancer, urinary bladder cancer, larynx cancer, leukemia, nonmelanocytic cancer, cancer of the nasal cavity and sinuses, and mesothelioma), important differences can be observed between Spain and other European countries (16). Although in these tumors it is accepted that occupational exposure causes an important proportion of all cancers, other risk factors (e.g., tobacco smoking, alcohol consumption, dietary patterns) or changes in the screening, diagnosis, and reporting of specific types of cancer could also explain some of the differences.

Lung Cancer

The estimated age-standardized incidence rate of lung cancer in males was 47.5 per 100,000 in 1990 (16). This means that Spain's incidence of lung cancer is one of the lowest in the European Union. However, the incidence and mortality is sharply increasing in men in Spain (17), which probably is mainly due to the strong increase in tobacco smoking, particularly from 1960 to 1975.

Urinary Bladder Cancer

The estimated incidence rate of urinary bladder cancer in males in 1990 in males was 21.3 per 100,000. Spain's incidence for this tumor is one of the highest in the

European Union (16). Specific mortality rates for men rose for all age groups from 1952 to 1986 (17).

Laryngeal Cancer

The estimated incidence rate for laryngeal cancer in men in Spain was 13.1 per 100,000 in 1991. Spain has the highest incidence of laryngeal cancer within the European Union (16). The male mortality rate shows an exponential rise until 65 years of age. These curves go into a gradual climb from the age of 40 onward (17).

Leukemia

The incidence rate of leukemia in males was 7.2 per 100,000 in 1990 (16). It is one of the lowest in the European Union. However, the trend of mortality from 1952 to 1986 is clearly upward, particularly in the older groups of men. The growing upward trend in Spain is much more pronounced than that seen in England and Wales (similar ranking to Spain) or in Italy (highest mortality) (17). The increase of mortality rates in Spain could be due to improvement in diagnostic accuracy as well as exposure to chemicals known to cause leukemia.

Nonmelanocytic Skin Cancer

The mortality rate (age standardized) of nonmelanocytic skin cancer in males was 2.03 from 1982 to 1986 (17). Although mortality fails to reflect the real incidence of skin tumors, trends of age-specific mortality in Spain reflect a special pattern. After an initial decline, they ultimately rise for nearly all age groups (17).

Cancer of the Nasal Cavity and Sinuses

This is also a rather infrequent tumor in Spain. From 1982 to 1986 the mortality rate in males was 0.29 per 100,000. A cohort effect of decrease in mortality was observed in generations from the beginning of the century, but a slight rise was observed in later generations (17).

Mesothelioma

National statistics on incidence and mortality from mesothelioma are not available in Spain. The mortality rate per 100,000 inhabitants for the province of Barcelona from 1983 to 1990 was 0.83 for males, which is a middle level of risk compared to other European countries (18). A slight rise in mortality rate was observed during this period although it was not statistically significant. In Spain the highest level of asbestos exposure was reached from 1970 to 1973 and as the latency period is between

20 and 40 years, the peak of asbestos effect (mesothelioma and lung cancer) is expected to be observed during the next 10 years.

Epidemiologic Studies on Cancer Risks and Occupation

Few studies have been conducted recently on occupational cancer in Spain. Etiologic studies are very unusual and record linkage studies using census data have not been done. Also, most of the studies have focused on confirming known associations. The most recent published studies, ordered according to the type of study, are the following:

Case Report Studies

A description of 34 cases of sino-nasal adenocarcinoma treated in Asturias between 1976 and 1992 (19) found a high prevalence of exposure to wood dust, an established risk factor for this tumor, in their working environment.

In relation to farmers exposed to organophosphorus pesticides in greenhouses, no significant decrease in the cholinesterase activity was observed in a small sample of 36 workers in Vizcaya and Guipúzcoa (20), but signs of poisoning were found in a study in Almería (10).

Ecologic and Death Certificate Studies

In the first systematic investigation on cancer in the agriculture industry in Spain, López-Abente (21) using a proportional mortality ratio approach found an excess of risk of hematolymphopoietic tumors, cancer of the brain, testis, prostate, and stomach, and a lower risk for lung cancer, cancer of the oral cavity, pharynx, larynx, and urinary bladder.

Similar results have been consistently reported from other studies, despite the large amount of missing data in death certificates in Spain (death certificates often do not include complete information on occupation), which indicates the usefulness of this type of study.

In a complementary case-control study (21) that was based on death certificates within the region of Castilla-León (a mostly rural area), a statistically significant increase of risk for stomach cancer, brain cancer (mainly in agriculture areas), lymphatic chronic leukemia, multiple myeloma, and non-Hodgkin lymphoma (in cattle areas) was found for the occupations in the agricultural industry.

Another proportional mortality study was done among steelworkers who died between 1986 and 1993 in the Basque

country (the Altos Hornos de Vizcaya steel mill) (22). Results showed a statistically significant excess of stomach cancer and renal cancer, as other authors have found. On the other hand, an excess of mortality risk from lung cancer, bladder cancer, and chronic respiratory diseases was not found, which could be due to classification and selection bias (high proportion of unknown causes of death and cancer of unspecified location).

In a study of socioeconomic differences in mortality in males who died between 30 and 64 years of age in eight provinces with high quality information on occupation in death certificates (23), the mortality in professionals and managers (group I) was compared with manual laborers (group II). The standardized mortality ratios (SMRs) were higher in group II, except for cancer of the colon and rectum.

In the province of Barcelona, the mortality from pleural mesothelioma, by municipalities, from 1983 to 1990 was studied (18). The geographic situation of the companies using asbestos in the province was also obtained. The calculation of SMRs for municipalities within the province showed a statistically significant increase in the risk of mesothelioma in two municipalities where there are companies producing asbestos cement.

Finally, a high incidence of thyroid neoplasms, soft-tissue sarcoma, and brain tumors was found in a village in Catalonia located in the vicinity of an organochlorinated compounds factory (24), which agrees with previously reported associations.

Case-Control Studies

The first published case-control study on occupational cancer in Spain was performed on bladder cancer among workers in the textile industry, in one area of Catalonia with an unusually high mortality rate for bladder cancer (14). The odds ratio (OR) for past employment in the textile industry was 2.2 and was higher (4.4) for subjects who worked in dyeing or printing and who were most probably exposed to azo dyes.

In a second larger, multicenter case-control study (13) on occupation and bladder cancer carried out in Barcelona, Madrid, Cadiz, Guipúzcoa, and Vizcaya, an increased risk of bladder cancer for men was found for textile workers (OR = 2.0; 95% confidence limits [CL] = 1.2–3.3); mechanics and maintenance workers (OR = 1.9; 95% CL 1.2–2.8), workers in the printing industry (OR = 2.1; 95% CL = 1.0–4.3); and for managers (OR = 2.0;

95% CL = 1.2–3.5). In females, the only increased risk was found for textile workers (OR = 6.4; 95% CL = 1.3–61.6). The risk was highest among those first employed in the textile industry before the age of 25 and prior to 1960. This study also found a multiplicative effect of cigarette smoking and occupational exposure to aromatic amines.

The association between occupational exposure and stomach cancer in Spain was investigated in a multicenter case-control study conducted in areas of Catalonia, Aragon, Castilia, and Galicia (25). An increased risk (adjusted for socioprofessional status and dietary habits) was found for coal mining workers (OR = 11.8), but the number of exposed workers was small (95% CL = 1.4–103). An increased risk was also observed for wood and furniture workers, construction workers, and glass and ceramic workers, but none of these risks were statistically significant. Taking into account all the occupations with potential exposure to different kinds of industrial dust (organic and inorganic dust) according to an occupational exposure linkage system, an increased risk of gastric cancer was found for occupations associated with exposure to silica and mineral dust (OR = 1.8; 95% CL = 0.9–3.6) (25).

The association between occupational exposure and laryngeal cancer was investigated in a small case-control study carried out in Madrid (26). An increased risk was found for woodworkers and furniture workers. The ORs for exposed workers who had worked in the industry for over 20 years were 5.6 (95% CL = 1.2–26.6) and 6.7 (95% CL = 1.1–42.6), respectively.

Finally, two case-control studies have been carried out in Spain to assess the influence of sun exposure. In a study in Valencia (27), open-air occupational activities were associated with an increased risk of nonmelanoma skin cancer; in another study in Granada (28), a statistically significant and positive trend was observed between the risk of cutaneous malignant melanoma and occupational sun exposure of the skin.

Cohort Studies

We were able to identify only two published cohort studies focusing on occupational exposure and cancer. One was conducted among workers in the pulp and paper industry in Catalonia (29). In a historic cohort using job histories and a company exposure questionnaire to assess the level of exposure, the SMR observed for all malignant neoplasms was 0.9 (95%

CL = 0.7–1.2). Excess risk was observed in females for mortality from all neoplasms (SMR = 1.7; 95% CL = 0.8–3.0) and breast cancer (SMR = 2.9; 95% CL = 0.8–7.3), and for large intestine cancer in both sexes (SMR = 2.9; 95% CL = 1.2–5.3).

The other retrospective cohort study (30) was conducted among 5,657 workers of the former Spanish Nuclear Energy Board to assess the effect of ionizing radiation exposure. Compared with that for the Spanish population, an excess mortality due to bone tumors was found for the cohort (SMR = 3.0; 95% CL = 1.1–6.4). Among miners high mortality from lung cancer was observed but bordered on statistical significance.

Present Problems and Main Challenges for the Future

Availability and Quality of Data

The situation in Spain is not favorable for occupational studies based on information from death certificates. The primary limitations are the availability of death certificates and the quality of the information on occupation in mortality statistics (31). Linkage studies developed in Nordic countries (32), which included occupational data taken from the population census, dates and causes of death taken from death certificates, and incident cancer cases taken from cancer registries, have never been done in Spain.

According to a study using data from 1981 and 1987 and comparing the quality of information on deaths recorded in Catalonia and Spain, the situation is getting worse (33). In 1981 the proportion of deaths of persons in Spain with no classifiable occupation was almost twice that of Catalonia. However, in 1987, in Catalonia, almost half the death certificates had no information on occupation (47.7%) and only 5.5% had detailed information. Classifiable occupation decreased from 30.9 to 11.3% between 1981 and 1987.

In Spain there is no national death index as there is in other countries. This is a serious limitation for retrospective and prospective epidemiologic cohort studies. For reasons of confidentiality, nominal information on the cause of death is not available from the National Institute of Statistics (Instituto Nacional de Estadística). It was possible previously to obtain the cause of death from the civil register but some years ago the civil register ceased registering the cause of death.

A recent paper shows the methodological problems found during the identification of workers' cohort in Altos Hornos del Mediterraneo, a Spanish iron foundry (34). With the collaboration of the enterprise, personnel files were obtained; 6% of cohort members were lost during the follow-up period, and 88% of causes of death were retrieved.

The Spanish registration system of occupational diseases is another example that shows the scarce attention paid to occupational problems and the health of workers. Despite the existence of an official list of occupational diseases since 1978 in Spain, including several cancers, there is serious underregistration. Although 258,485 occupational diseases were reported in 1985 in Italy, only 3100 were reported in Spain (35). The register does not reflect the whole impact of occupational risk factors on workers' health.

Shortage of Funds

Human and financial resources in occupational cancer research are insufficient. This unfavorable situation is illustrated by considering the number of studies and the distribution of money from the main financial research agency in Spain.

According to one of the latest reports published by the Health Research Fund of the Ministry of Health (36) in 1993, 64 proposals in the field of cancer were selected to be funded for a total amount of 1.2 million ecus. Only two of these projects were occupational or environmental studies.

Application of New Strategies and Methods, and Priorities for Future Research

There are two problems in the field of occupational cancer: risk identification and risk management. Regarding risk identification, it is clear that Spain is one of the developed countries that has had a possible decrease in the rate of identification of new occupational carcinogens (32). Several changes have occurred over the last few years; chemical agents have been substituted and industrial processes have changed. Lower doses of exposure and new employment conditions where workers perform multiple tasks make it more difficult today to determine a close correspondence between a specific job exposure and a job title (31).

Future research in the identification of risk should be directed toward exposures without enough evidence in humans but with sufficient evidence in animals (IARC

Groups 2A and 2B). Research cannot be limited to repeating what has been done in other countries. Interesting new hypotheses can be investigated, preferably in industrial areas or in jobs with higher exposures.

Improvement in the methods of assessment of exposures are needed. The use of expert hygienists in the evaluation of the exposure is very limited in Spain and could be extended. It is also necessary to improve the use of new methods such as the biochemical and biologic markers used in the assessment of exposure and diseases.

Preventive measures for managing risk of occupational cancer in Spain are still insufficient. Reduction of cancer by limiting or avoiding exposure to known occupational carcinogens is still necessary. Protection of workers from the risk related to exposure to carcinogens remains the most effective way of controlling occupational cancer.

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